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AGE RELATED MALE PROBLEM: ACUTE AND CHRONIC BACTERIAL PROSTATITIS

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ABSTRACT

Prostatitis is the inflammation of the prostate, characterized with persistent pain with or without urogenital symptoms. Prostatitis can be divided into four major groups: acute bacterial prostatitis, chronic bacterial prostatitis, prostatitis/pelvic pain syndrome (CP/CPPS) and asymptomatic inflammatory prostatitis. Prostatitis is the most common urological presentation in men above 50 years of age, when enlargement of prostate gland interferes with emptying of bladder. The diagnosis, pathogenesis and treatment of prostatitis continue to be challenging to the urologists. Prostatitis has a significant impact on quality of life. Drugs of choice would be appropriate with bacteremia caused by gram-negative bacilli and gram-positive cocci. Many drugs that do not penetrate into prostrate under normal conditions are effective in acute bacterial prostatitis. Long term treatment and follow up with repeated microbiologic evaluations is needed that patients respond to treatment.

KEYWORDS: Prostatitis, Chronic Pelvic Pain Syndrome, Treatment

INTRODUCTION

Prostatitis is the inflammatory disorder due to chronic bacterial infection, which is characterized bychronic or recurrent urogenital symptoms in the setting of documented or suspected bacterial infection of the prostrate [1]. It has been estimated that 50% of men experience symptoms of prostatitis at some time in their lives. Studies have suggested that the prevalence of prostatitis is 2% to 16% [2]. In otherwise healthy young men; prostatitis may be the most common urologic diagnosis. In the United States there were almost 2 million visits annually for prostatitis, accounting for 8% visits to urologist and 1 % visits to primary care physicians and the cost of prostatitis is about $ 84 million annually [3,1]. Prostatitis has a significant impact on the quality of life (QoL) comparable to Crohon's disease or a recent myocardial infarction[4]. Prostatitis is the most common urological diagnosis in men < 50 years of age and is third most common diagnosis among those 50 years of age [3]. Tripp *et al* [5] reported the prevalence of chronic prostatitis (CP) like symptoms in 264 Canadian adolescents aged 16-19 years (mean age 17.5, sd 1.1) was 8.5%, with 3% reporting moderate-severe CP like symptoms. Ferris*et al* [6] using National Institutes of Health Chronic Prostatitis Symptoms Index(NIH-CPSI) estimated prevalence for urogenital pain in Australian men aged 16-64 years was 8%(1373); an estimated 3% of men experienced pain from more than one urogenital location. The estimated prevalence of prostatitis-like symptoms in Australian men was 2%. In a large recent review by Krieger *et al* [7] the prevalence of prostatitis symptoms in 10,617 men was 8.2%(823).Amongst these patients the prevalence of prostatitis symptoms ranged from 2.2 % to 9.7%,with a median rate of 8.7%. Men with prostatitis symptoms appear to be at increased risk for persistent symptoms and for recurrent episodes. Although the pathogenesis is still being evaluated, it is common clinical practice to see patients recurrently with acute episodes of prostatitis with a background of chronic prostatitis. These patients hence have a substantially higher cumulative probability of subsequent episodes of prostatitis [8]. Prostatitis symptoms may be classified into four major groups: acute bacterial prostatitis, chronic bacterial prostatitis, chronic prostatitis/chronic pelvic pain syndrome and

asymptomatic inflammatory prostatitis [9]. Common pathogens isolated in the bacterial prostatitis include: Enterobacteriaceae, Pseudomonas, *Chlamydia trachomatis, Neisseria, gonorrohoeae, Mycobacterium tuberculosis* and variousfungi. Therapy of chronic prostatitis requires prolonged treatment with an antibiotic that penetrates the prostrate (i.e., one with high lipid solubility, a low degree of ionization, high dissociation constant low protein binding, and small molecular size [10]. Quinolones are the antibiotics of choice for treating bacterial prostatitis. This paper reviews the acute, chronic bacterial prostatitis and chronic pelvic pain syndrome.

PROSTATITIS

Prostatitis symptoms may be those of cystitis with dysuria, frequency, and urgency, or symptoms of bladder outlet obstruction may predominate, with hesitancy, diminished stream, nocturia or postmicturition dribbling. Perineal or low back pain may, onoccasion, be the only manifestation. Physical examination findings that help differentiation acute from chronic prostatitis Examination should include inspection and palpation for evidence of ureteral discharge, penile lesions, local epididymal or testicular disease, and inguinal adenopathy [11]. Organisms that ascend through urethra cause most infections of the urogenital ducts and accessary sex organs. Mechanical factors, such as the flushing action of micturitionand ejaculation, should provide some protection against infection, although the relative significance of these defenses is unclear [12]. A zinc containing polypeptide termed the *prostatic antibacterial factor* is the most important antibacterial substance secreted by the prostrate. Men with well-documented chronic bacterial prostatitis have significantly lower levels of zinc in their prostatic fluid than healthy men, but their serum zinc levels are within normal limits. Other finding suggest that bacterial prostatitis and chronic prostatitis/chronic pelvic pain syndrome are associated with prostatic secretory dysfunction [13]

In order to standardize definition, improve diagnosis and treatment, and facilitate research, the United States National Institutes of Health (NIH) established an International Prostatitis Collaborative Network to devise a classification approach for prostatitis [9]. The scheme developed by this group is currently accepted categorization of prostatitis and defines: 1) Acute bacterial prostatitis-Acute urogenital symptoms with evidence of bacterial infection of the prostrate. 2). Chronic bacterial prostatitis (CP)-Chronic or recurrent urogenital symptoms with evidence of bacterial infection of the prostrate.3, a).Chronic prostatitis/chronic pelvic pain syndrome(CPPS), inflammatory-Chronic or recurrent urogenital symptoms with evidence of inflammation, but not bacterial infection of the prostrate. 3,b)Chronic prostatitis/chronic pelvic pain syndrome, non-inflammatory-Chronic or recurrent urogenital symptoms without evidence of inflammation or bacterial infection of the prostrate(formerly designated prostatodynia).4). Asymptomatic inflammatory prostatitis-Absence of urogenital symptoms with evidence of inflammation of the prostrate found incidentally (e.g. biopsy performed for different purpose).Evidence of inflammation or bacterial infection is usually determined by the presence of inflammatory cells in, or bacterial growth from, expressed prostatic secretions, post- prostrate massage urine, or seminal fluid. Maneuvers performed in the urology office can help define the categorization of patients. As an example, including post-massage urine and seminal fluid for assessment of inflammatory cells effectively doubles the number of people in the inflammatory subset (compared with using purulent prostatic secretions alone) [14].

PATHOGENESIS

The etiology and pathophysiology of CP/CPPS remains a mystery, although central neurological mechanisms probably play a role. Patients with PPS show no evidence of infection; they do not have urethritis, urogenital cancer, urethral stricture, or neurologic disease involving the bladder, and they do not exhibit any overt tract disease [15]. The initial concept of infection and inflammation arose when True *et al* [16]. analyzed the outcome of Prostrate

histopathology in 368 biopsies from 97 patients with CP/CPPS. In these patients prostatic inflammation was detected in only 33% of patients, including 29% with mild(less than 10 leukocytes per mm. field) and 4% with moderate (between 10 and 200) or severe (more than 200) infiltrate. Of the 3 patients with moderate inflammation 1 had glandular, 1 periglandular and 3 multifocal or diffuse distribution of leukocytes in the interstitium. Although 33% patients had inflammation on prostrate biopsies, only 5% of 97 patients had moderate to severe inflammation. This study questioned the association and role of inflammation in the pathogenesis of CP/CPPS. Despite this CP/CPPS continues to be diagnosed on the basis of symptoms. It is diagnosed from a history of persistent genitourinary pain and an absence of other lower urinary tract pathologies. The severity of disease, its progression and treatment response can be assessed only by means of a validated symptoms-scoring instrument [17, 18].

Patients with CP/CPPS are diagnosed traditionally using gold-standard four-glass test for bacterial localization [18]. However, as this test is cumbersome to perform and hence the diagnostic efficiency may be enhanced cost effectively by simple screening procedure ,that is, two- glass test, or by pre-and post-massage test(PPMT),with PPMT able to indicate the correct diagnosis in>96% of patients [19,20]. These tests use the White blood cells (WBC) as marker on inflammation. White blood cells can be found in seminal plasma and prostatic fluid of asymptomatic patients and in patients with pelvic pain [21].Schaeffer *et al*[21] in a study examined 488 men, whether leukocytes and bacteria correlate with symptom severity in men with chronic prostatitis. Chronic pelvic pain syndrome The authors concluded that men with chronic prostatitis routinely receive anti-inflammatory and antimicrobial therapy despite leukocytes and bacterial counts which do not correlate with severity of symptoms. These findings suggest that factors other than leukocyte and bacteria also contribute to symptoms associated with chronic pelvic pain syndrome. Based on current studies the initiation of the inflammatory process in CP/CPPS within the prostrate is thought to be a local infection, chemical irritation, dysfunctional voiding, intraductal reflux, neuromuscular disturbances or an immunologic process. Regardless of the triggering factors, the resultant inflammatory process causes tissue edema and increased intra-prostatic pressure leasing to local hypoxia and varied mediator-induced tissue damage. This leads to altered neurotransmission in sensory nerve fibers thereby resulting in the pain and other symptoms associated with the condition [22]. Nikhil *et al* [23].presented the common etiologies associated with CP/CPPS include: 4A) Infection,4B) Inflammation and autoimmunity, 4C) Neurological, 4E) Psychological and 4F) additional conditions.

The acute and chronic bacterial prostatitis is mainly caused by the organisms responsible for urinary tract infections (UTI). Additionally bacteria responsible for both acute and chronic prostatitis include *Pseudomonas* and *Streptococcus faecalis*. The symptoms of CP/CPPS are identical to those od prostatic infection [23] Blacklock *et al* [24] noted that some patients with CP/CPPS had some pathogens identified in vaginal secretions of their sexual partners. Magri *et al* [25] evaluated 55 symptomatic patients with CP/CPPS they were subjected to segmented tests to localize *Chlamydia trachomatis* in first voided urine(VB1),prostatic secretions(EPS),post massage voided(VB3) or semen specimens. In a landmark paper evaluating the link between autoimmunity and CP /CPPS, Kouiavskaia *et al* [26] aimed to assess whether T cells from a group of men with CP /CPPS would recognize peptides derived from normal self-prostatic proteins prostate specific antigen (PSA)and prostatic acid phosphatase (PAP). The authors used purified CD4 T cells from the peripheral blood of 31 patients with CP /CPPS. This study demonstrated a strong link between autoimmunity and CP /CPPS in that CD4 cells from patients with CP /CPPS had higher frequency of recognition and the self-prostatic proteins PAP and PSA compared to normal male blood donors.

CLINICAL MANIFESTAIONS

Acute Bacterial Prostatitis

Manifestation of acute bacterial prostatitis is seldom subtle or difficult diagnosis. Patients complain of symptoms associated with lower urinary tract infection, such as urinary frequency and dysuria. Patients may also experience lower urinary tract obstruction caused by acute edema of prostrate. Signs of systemic toxicity are common. Some patients have had recent genitourinary procedures [27, 28]. On physical examination patients may have a high temperature and lower abdominal or suprapubic discomfort caused by bladder infection. Findings on rectal examination are frequently impressive, with an exquitely tender, tense prostrate on palpation. Results of urine examination are abnormal, with pyuria, and cultures are positive. Bacteremia may be present spontaneously or may result from excessively vigorous rectal examinations. Gram negative uropathogens especially *Escherichia coli* are causative agent in more than 60% of cases [29, 28]. Antimicrobials are administered after specimens have been obtained for urine and blood cultures. Urinary retention is managed best with a suprapubic cystostomy rather than atransurethral catheter, to ovoid obstructing drainage of infected prostrate secretions into urethra. General measures, including hydration, analgesics, and bed rest, also are indicated. The most important complications of acute bacterial prostatitis are prostatic abscess, prostaticinfarction, chronic bacterial prostatitis and granulomatous prostatitis [12].

Chronic Bacterial Prostatitis

Chronic bacterial prostatitis is an important cause of bacterial persistence in the lower urinary tract. Characteristically patients experience recurrent bacterial urinary tract infections caused by the same organism [9].Patients often are asymptomatic between episodes of bladder bacteriuria. The prostate gland is usually normal on rectal or endoscopic evaluation. Careful lower urinary tract localization studies constitute the cornerstone on which to base a diagnosis of chronic bacterial prostatitis. Evaluation of the pre-and post-prostrate massage samples has been proposed as an alternative to the traditional lower urinary localization study [30]. Diagnosis of chronic bacterial prostatitis based on symptoms, the number of leukocytes in expressed prostatic secretions, or the use of prostrate biopsy specimens is adequate [11]. Gram- negative rods, members of Enterobacteriaceae or Pseudomonas are the most important pathogens in chronic bacterial prostatitis. Gram- positive cocci, such as *Enterococcus faecalis* or Staphylococci, may be causative organisms in few cases [31]. However, recent studies have suggested that gram-positive localization are often are not repeatable in untreated patients [32]. Bacteria isolated from patients with chronicbacterial prostatitis even after multiple episodes of symptomatic bacteriuria and prolonged courses of antibiotics, are often antibiotic sensitive strains [13]. *E. coli* strains that cause prostatitis tend, however, to possess urovirulence profiles similar to strains isolated from women with acute pyelonephritis, especially hemolysin and cytotoxic necrotizing factor, with many strains exhibiting multiple virulence factors [33].

Chronic Prostatitis /Chronic Pelvic Pain Syndrome

Patients with chronic prostatitis /pelvic pain syndrome are the largest population of patients with prostatitis, representing more than 90% of patients evaluated. Studies have shown that CPPs causes substantial morbidity and substantially decreases patients QoL[34]. These patients may complain of various perineal and pelvic symptoms, especially pain [35]. Pain or discomfort may be perineal, suprapubic, infrapubic, penile, scrotal or inguinal in location. Other complains include voiding difficulty and erectile dysfunction. The discomfort may be described as either continuous or spasmodic and commonly is described as “dull ache”. Patients may complain of urinary symptoms. Ejaculation complains and sexual dysfunction are common [36]. The causes of CPPS are uncertain and subject to ongoing debate.

Mardh and Colleen and Mardh and associate have found no evidence for a causative role for *Neisseria gonorrhoeae, Trichomatis vaginalis, Ureaplasa urealyticum, Mycoplasma hominis, Candia albicans, anaerobicbacteria, Chlamydia trachomatis*, or viruses in these syndrome [21, 37]. Other researchers have reported however, that many patients with sub-acute or chronic prostatitis are infected with gram-positive bacteria *trachomatis, or U. urealyticum* [3, 38, 9]. The techniques, control groups, and findings in these later studies have been questioned by other workers[13]. Molecular studies have shown that patients with inflammatory CPPs are significantly more likely to have bacterial DNA in prostatic secretions than patients without inflammation or control patients with prostate cancer [39, 40].

Asymptomatic Inflammatory Prostatitis

NIH consensus classification of prostatitis includes a category for patients who have a diagnosis of prostatitis but who have no genitourinary tract symptoms [12]. These patients have prostrate inflammation but have none of the usual symptoms associated with other prostatitis syndromes. It is common for patients with elevated prostate-specific antigen levels to undergo prostrate biopsy for evaluation of possible prostate cancer. The common benign pathologic diagnosis is prostatitis, basedon the histologic findings of inflammatory infiltrates in the prostatic parenchyma. Some clinicians recommend a course of antimicrobial or anti-inflammatory therapy in this situation. [41].

Prostatic Abscess

Prostatic abscess is a rare complication. Most prostatic abscesses occur in patients with diabetes, in immune compromised patients, and in patients who have not received appropriate therapy for acute prostatitis. Foreign bodies and urinary tract obstruction are other predisposing factors. In the past, *N. gonorrhoeae* was a common pathogen, but most cases now are caused by the ascending route. Occasionally, *S.aureus* is the pathogen, which suggests the possibility of hematogenous infection. Blastomycoses, cryptococcosis and nocardiosis are also well described causes of prostatic abscess [12].

Granulomatous Prostatitis

Granulomatous prostatitis is a characteristic histologic reaction of the prostate to various insults, with granulomas containing lipid-laden histocytes, plasma cells, and scattered giant cells. In most cases, granulomatous prostatitis follows and episode of acute bacterial prostatitis [42].There also are many specific infectious causes of granulomatous reaction by the prostate.Tuberculous prostatitis usually is secondary to tuberculosis elsewhere in the genital tract [43]. Most patients have no symptoms referable to prostatic infection. Atbiopsy, the granulomas may contain typical Langerhans giant cells and exhibit caseous necrosis. These infections are caused most often by *Mycobacterium tuberculosis*, butalso have been reported with nontuberculos mycobacteria. Iatrogenic mycobacterial prostatitis may develop in patients who receive intravascular Calmette-Gue'rin bacillus treatment of transitional cell carcinoma of the bladder. Prostatitis may be secondary to systemic involvement of many of the deep mycoses [44]. Most cases of mycotic prostatitis reported have been associated with blastomycosis, Coccidioidomycosis, and cryptococcosis [45].

TREATMENT

The treatment of CP /CPPS remains uncertain, and have been divided into Urological treatment into medical and surgical categories [23]. The predominant medical treatment of drugs include: a) antibiotics) alpha blockers) Anti-inflammatories, d) 5α reductase inhibitors) pentosulphan polyphosphate and additional therapies. The urological surgery treatment include:1) prostatic massage, 2) transurethral microwave therapy, 3) transurethral resection of prostate

Many drugs do not penetrate into prostate under normal conditions are effective in acute bacterial prostatitis.

Drugs that would be appropriate in patients with bacteremia caused by Enterobacteriacaea, pseudomonas and enterococci should be administered [12]. Depending onthe results of antimicrobial sensitivity, the preferred therapy is at least 4 to 6 weeks with an oral fluoroquinolone, which results in microbiological cure rates 70% or more in recent years [46]. Long-term follow up with repeated microbiologic evaluations is needed to ensure that patients respond to treatment [12].

CONCLUSIONS

Pathogenesis and diagnosis of chronic bacterial prostatitis is well defined, but our knowledge on asymptomatic prostatitis is limited.Fluoroquinolones are the only effective antimicrobials for bacterial prostatitis. The current generation of quinolones will not maintain the efficacy indefinitely; we need to find other agents that penetrate prostrate.

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